

# Sequential left internal mammary artery grafting in combination with the aortic no-touch technique



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## Abstract

**Aim:** This study aimed to investigate the short-term outcomes achieved with off-pump bypass combined with the aortic no-touch technique where sequential anastomoses between the left internal mammary artery (LIMA), left anterior descending (LAD) and diagonal artery were employed.

**Material and methods:** A total of 583 patients (mean age 63, 80% male) who underwent off-pump bypass (LIMA-diagonal-LAD sequential) were enrolled in this retrospective analysis. Data regarding the frequency of in-hospital postoperative complications, intra-aortic balloon pump (IABP) and inotropic agent requirement, re-exploration for bleeding, and length of hospital stay were collected. Anastomosis patency was evaluated in 49 patients who underwent angiography.

**Results:** 2.6% of the participants received inotropic agents and 0.5% required IABP. Frequency of acute renal failure, sternal wound infection, cerebrovascular event, respiratory failure, and hemodialysis was less than 1% in total. Among the 49 patients undergoing angiography at an average 41 ±17 months after bypass, the LIMA-LAD was patent in 98% and the LIMA-diagonal was patent in 84% of the subjects. Preoperative left ventricle ejection fraction (LVEF) and recent myocardial infarction (MI) prior to bypass were significantly correlated with postoperative IABP and inotropic agent requirement ( $r = 0.165$ ,  $p < 0.01$  for LVEF,  $p = 0.021$  for recent MI).

**Conclusions:** Off-pump bypass in combination with the aortic no-touch technique is associated with favorable postoperative outcomes including reduced postoperative stroke, renal dysfunction, IABP, and inotropic agent requirement compared to the results of previous randomized prospective studies published in the literature.

**Key words:** stroke, aortic no-touch, sequential grafting, off-pump coronary artery bypass graft.

## Introduction

Coronary artery bypass graft (CABG) surgery is one of the most heavily scrutinized surgical procedures performed worldwide. Despite this, many questions regarding optimal strategies for reducing perioperative morbidity remain unanswered. Postoperative stroke is a rare but devastating complication of CABG surgery, occurring in approximately 1.5–3.5% of all procedures [1]. Because it is the only major cardiovascular complication where percutaneous coronary intervention has shown an advantage over CABG, it is essential to study postoperative stroke and minimize its occurrence. As stroke is such a devastating complication of CABG surgery, this finding has been used by some clinicians as a reason to push patients toward percutaneous coronary intervention (PCI) [2]. The main argument against

CABG is the higher incidence of stroke when compared to PCI [3]. However, the inferior neurological outcomes reported in previous studies resulted from the preferred use of conventional CABG strategies requiring cardiopulmonary bypass (CPB) and aortic cross-clamping techniques, all well-known predictors for worse neurological outcomes [4].

The majority of CABG procedures are performed with the use of cardiopulmonary bypass, which in almost all cases implies cannulation and clamping of the ascending aorta. Depending on the strategy for proximal anastomosis, the aorta may be clamped only once, or a second time using a partial clamp. Off-pump CABG (OPCAB) gives the surgeon more freedom to dictate the degree of aortic manipulation. Often, a partial aortic clamp is used to allow proximal anastomoses to be sewn in a bloodless field.

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However, aortic clamping can be avoided completely with the use of clampless facilitating devices or proximal anastomotic connectors. Finally a no-touch technique that was associated with nearly 60% lower risk of postoperative cerebrovascular events as compared to conventional side-clamp OPCAB with the effect consistent across patients at different risk can be employed in which aortic manipulation is avoided completely by providing inflow to all grafts from one or two in-situ internal mammary arteries, sequential anastomosis or employing a hybrid approach when clinically appropriate [5].

We often need to revascularize multiple targets in patients with increasing severity of disease. Sequential arterial grafting is a useful procedure to achieve effective revascularization in these patients with a limited number of grafts [6–9]. The IMA pedicled graft which carries its homeostatic milieu with it [10] has been demonstrated to improve survival after coronary artery bypass grafting [11]. The excellent reported results of bilateral, sequential, and free IMA grafting, although mostly performed in selected patients, have enhanced this conduit's versatility [12].

### **Aim**

In our institutions, we nearly only perform OPCAB and always try not to touch or minimally touch aorta by using all combinations of composite T/Y arterial grafts and sequential anastomoses, when clinically appropriate.

In our institutions, from 2008 to 2016 we performed 19 461 open heart surgery operations. Of these, 15 568 were pure coronary artery bypass procedures.

As part of this approach, the present study aimed to investigate short-term postoperative outcomes achieved with OPCAB combined with the aortic no-touch technique, where sequential anastomosis between the left internal mammary artery (LIMA), left anterior descending artery (LAD) and diagonal artery was employed when clinically appropriate.

Written informed consent was obtained from all patients and the study was approved by the institutional review board (our institute – Clinical Research Ethics Committee, date: 23.03.2015, no: 21/16).

### **Material and methods**

Medical records concerning the demographic features, postoperative complications, and length of hospital stay of 583 patients who underwent OPCAB (LIMA-diagonal-LAD sequential), when clinically appropriate, between January 2008 and January 2016 in our institutions, were retrieved from the institutional electronic database. Those with cardiogenic shock and renal or hepatic failure on admission, emergency CABG and redo CABG were not included in the statistical analysis. Carotid artery Doppler ultrasound was routinely performed on all patients before surgery. Those with stenosis of 70% or more in the carotid artery were not included in the study. All transient ischemic attacks (defined as resolving completely within 24 hours), strokes (defined as focal or global cerebral dysfunction of presumed vascular origin lasting more than 24 hours) were included.

The patients with only both 70% and above proximal, distal or mid stenosis in the LAD and diagonal branch were selected by the same team of surgeons.

### **Surgical technique**

All CABGs were performed by the same surgical team in a standardized fashion. Arterial and venous catheters were inserted into the radial artery and right jugular vein before sternotomy. Blood pressure, central venous pressure, urine output and oxygenation were monitored throughout the surgery. All patients underwent standard median sternotomy under general anesthesia. Grafts were prepared after heparinization (300 IU/kg). After placement of the Favaloro retractor, the LIMA was harvested in the form of pedunculated grafts using electrocautery and hemoclips. During and after harvesting of the LIMA, a warm papaverine solution was used to prevent LIMA spasm. Stabilization of target coronary arteries was achieved via four myocardial radial traction sutures as described in detail previously [13, 14] and no commercial stabilization system was used. Intracoronary shunts were not used, while a bloodless field was obtained by occlusion of the proximal target vessel by lightweight bulldog clamps and visualization was aided with constant saline squirting during the anastomosis. Following the performance of side-to-side LIMA-diagonal artery anastomosis, coronary flow in the distal LAD was checked and end-to-side LIMA-LAD artery anastomosis was carried out using 8-0 prolene sutures. Systolic blood pressure was kept between 50 and 60 mm Hg and the heart rate was decreased to 50–60 per minute.  $\beta$ -blocker agents, Trendelenburg positioning and crystalloid volume replacements were used as needed according to the hemodynamics of patients. None of the patients received inotropic agents during the stabilization and had decompensation. Following the operation, patients were transferred to the intensive care unit (ICU) and received enoxaparin (0.1 mg/kg) twice daily for three days. From the first postoperative day, all patients were started on a lifelong daily maintenance dose of 100 mg of acetylsalicylic acid.

Data regarding the frequency of in-hospital postoperative complications, intra-aortic balloon pump (IABP) and inotropic agent requirement, re-exploration for bleeding, and length of hospital stay were collected from medical records. In addition, the patency of the LAD and diagonal arteries was evaluated in 49 patients who underwent subsequent coronary angiography in our institutes.

### **Statistical analysis**

All statistical analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was used to determine whether variables are normally distributed. Data are given as mean  $\pm$  standard deviation or median (1<sup>st</sup> quartile – 3<sup>rd</sup> quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. Correlation analysis and  $\chi^2$  tests were performed to identify the association between selected outcomes and the demographic features of

**Table I.** Demographic and clinical characteristics of the study population ( $n = 583$ )

Parameter	Value
Age [years]	63.0 (55.0–72.0)
Gender, male	470 (80.61%)
Recent MI, $n$	223 (38.25%)
Hypertension, $n$	323 (55.40%)
Diabetes, $n$	246 (42.19%)
Smoking, $n$	319 (54.71%)
Family history of CAD, $n$	323 (55.40%)
Cerebrovascular disease, $n$	25 (4.28%)
LVEF %	50.0 (45.0–55.0)

Data are given as median (1<sup>st</sup> quartile – 3<sup>rd</sup> quartile) for continuous variables, and as frequency (percentage) for categorical variables. CAD – coronary artery disease, LVEF – left ventricular ejection fraction.

**Table II.** Postoperative findings and complications ( $n = 583$ )

Parameter	Value
IABP insertion, $n$	3 (0.5%)
Inotropic agent requirement, $n$	15 (2.6%)
Revision for bleeding, $n$	12 (2.1%)
Acute renal failure, $n$	4 (0.7%)
Sternal wound infection, $n$	6 (1%)
Cerebrovascular event, $n$	4 (0.6%)
Respiratory failure, $n$	5 (0.9%)
Hemodialysis, $n$	4 (0.7%)
ICU stay [days]	1 (1–1)
Hospital stay [days]	5.0 (4.0–6.0)
Hospital death	1 (0.17)

Data are given as median (1<sup>st</sup> quartile – 3<sup>rd</sup> quartile) for continuous variables, and as frequency (percentage) for categorical variables. IABP – intra-aortic balloon pump, ICU – intensive care unit.

**Table III.** Correlation analysis and  $\chi^2$  test results demonstrating the association between postoperative complications and selected preoperative variables

	IABP		Inotropic agent		ARF		Respiratory failure	
	$r$	$p$	$r$	$p$	$r$	$p$	$r$	$p$
LVEF	-0.165		-0.238	< 0.001	-0.030	0.472	-0.072	0.082
Age	0.033	0.432	0.022	0.603	0.056	0.180	0.024	0.557
	$\chi^2$	$p$	$\chi^2$	$p$	$\chi^2$	$p$	$\chi^2$	$p$
MI	6.502	0.021	8.023	0.006	0.299	0.505	1.010	0.376
Diabetes	0.101	0.751	0.126	0.794	0.101	0.563	0.655	0.645

ARF – acute renal failure, IABP – intra-aortic balloon pump, LVEF – left ventricular ejection fraction, MI – myocardial infarction,  $\chi^2$  – Pearson  $\chi^2$ .

the study population. A  $p$ -value < 0.05 was considered to indicate statistical significance.

## Results

A total of 583 patients (mean age 63 years, 80% male) were enrolled in this retrospective study. Of the patients, 80.61% (470) were male, 19.39% (113) were female. The rates of recent MI, family history of CAD and cerebrovascular disease were 38.25% (223), 55.40% (323), 4.28% (25), respectively. The rates of hypertension, diabetes and smoking were 55.40% (323), 42.19% (246) and 54.71% (319), respectively. The mean LVEF of patients was  $48 \pm 9$ . Demographic features of the study group are presented in Table I. Following CABG, 2.6% (15) of the participants received inotropic agents and 0.5% (3) required IABP insertion. Frequency of acute renal failure was 0.7% (4); none of them returned to chronic renal failure. Frequency of sternal wound infection was 1% (6), respiratory failure 0.9% (5), hemodialysis 0.7% (4) and cerebrovascular event 0.6% (4). However, 2.1% (12) of the study subjects underwent revision surgery for excessive bleeding. Frequency of hospital death was 0.17% (1). Mean length of intensive care unit stay was  $1.4 \pm 1.8$  days and hospital stay including the intensive care unit was  $5.4 \pm 3.1$  days (Table II).

Correlation analysis and Pearson  $\chi^2$  test results indicated that preoperative LVEF and recent MI prior to

**Table IV.** Patency rate of the LAD and diagonal artery ( $n = 49$ )

Variable	Value
Time to coronary angiography [months]	41 $\pm$ 17
LIMA-LAD anastomosis patency, $n$	48 (98%)
LIMA-diagonal anastomosis patency, $n$	41 (84%)

Data are given as mean  $\pm$  standard deviation for continuous variables, and as frequency (percentage) for categorical variables. LAD – left anterior descending, LIMA – left internal mammary artery.

CABG were significantly correlated with postoperative IABP requirement ( $r = -0.165$ ,  $p < 0.01$  for LVEF,  $\chi^2 = 6.502$ ,  $p = 0.021$  for recent MI) and also inotropic agent requirement  $r = -0.238$ ,  $p < 0.001$  for LVEF,  $\chi^2 = 8.023$ ,  $p = 0.006$  for recent MI, Table III). As shown in Table IV, among the 49 patients who later underwent coronary angiography, the LIMA-LAD anastomosis was patent in 98% (48) and the LIMA-diagonal anastomosis was patent in 84% (41) of the subjects.

## Discussion

The detrimental effects of CPB and aortic manipulation have already been well demonstrated. Stroke is a devastating complication that increases morbidity, mortality and hospital stay and is the most prominent factor that some clinicians use to push the patients toward PCI even if the patient deserves CABG. Depending on the definition and

accuracy of diagnosis, the incidence of stroke associated with coronary artery surgery varies widely, between 1% and 4% [15, 16].

The present study demonstrates that off-pump CABG with sequential LIMA-diagonal artery-LAD anastomosis with the aortic no-touch technique is associated with favorable postoperative outcomes including reduced postoperative stroke, renal dysfunction, IABP, and inotropic agent requirement compared to the results of previously published randomized prospective studies. Preoperative LVEF and presence of recent myocardial infarction were significantly associated with the postoperative need for IABP insertion and inotropic agent requirement and prevalence of acute renal failure. The length of ICU stay and hospital stay reported in this study are also comparable with the results of the previous studies. Coronary angiography findings, which were performed in a minority of our study population, revealed that off-pump surgery combined with the aortic no-touch technique provides excellent LIMA-LAD anastomosis at an average of two and a half years after CABG. However, coronary angiography findings for LIMA-diagonal anastomosis are slightly higher than in the literature [17]. In our study, we observed that atherosclerosis progressed in the native vessel in patients with LIMA-diagonal occlusion, which we think contributes to the high occlusion compared to the literature. However, no patient with an occluded diagonal anastomosis was found to have an occlusion of the LIMA-LAD anastomosis. With this technique, we can safely say that the LIMA-LAD anastomosis is not compromised even if there is occlusion in the diagonal anastomosis. We think that sequential anastomosis contributes to graft patency, as demonstrated in the study by Li *et al.* [18].

Instrumentation of the aorta and lack of maintenance of proper cerebrovascular perfusion during CABG are the potential causes of postoperative stroke observed after CABG [19].

Off-pump CABG with the aortic no-touch technique using either composite arterial grafts or sequential anastomosis is unique with regard to the absence of instrumentation on the aorta and rapid performance of anastomosis [20, 21]. In a recent meta-analysis of 100 studies with an overall total of 19 192 subjects, Kowalewski *et al.* reported that off-pump CABG compared to conventional CABG was associated with a significant 28% reduction in stroke occurrence within 30 days of the surgery. The authors also reported that all-cause mortality and prevalence of postoperative MI were similar in these two techniques [22]. In another meta-analysis of 18 studies with 25 163 patients, off-pump CABG with the aortic no-touch technique was found to lead to a 60% lower risk of short-term ( $\leq 30$  day) postoperative cerebrovascular events compared to side-clamp off-pump CABG [5]. In our study, the prevalence of in-hospital stroke (0.6%) was lower than the reported prevalence of stroke in the meta-analysis by Kowalewski *et al.* (1.34%) but slightly higher than that reported in the meta-analysis carried out by Pawliszak *et al.* Nevertheless, our results show that off-pump CABG with the aortic no-

touch technique is associated with a significant reduction in the postoperative stroke rate when compared with on-pump CABG or off-pump CABG with a side-clamp, in which stroke rates are reportedly 5% and 1.3%, respectively.

In-hospital mortality occurred in 1 (0.17%) of the study patients enrolled in our study, which was much lower than the reported in-hospital mortality rate in previous randomized prospective studies and meta-analyses. The in-hospital all-cause mortality rate among patients undergoing off-pump CABG with the aortic no-touch technique in the meta-analyses carried out by Pawliszak *et al.* and Kowalewski *et al.* were 1.19% and 2.04%, respectively [5, 22].

The need for IABP insertion and inotropic agent requirement and prevalence of acute renal failure in our study group were 0.5%, 2.6%, and 0.7%, respectively. These results indicate that off-pump CABG with the aortic no-touch technique provides adequate myocardial perfusion and hemodynamic stability during and after surgery. In addition to the lack of unfavorable effects of cardioplegia on myocardial function, sequential side-to-side anastomosis provides better arterial flow compared to side-to-end anastomosis, which might be associated with the favorable hemodynamic outcomes observed in our study population [23]. Consistent with the evidence reported in previous studies, our findings indicate that preoperative LVEF and presence of recent myocardial infarction were significantly associated with the postoperative need for IABP insertion and inotropic agent requirement, and prevalence of acute renal failure [24].

The anastomosis patency rates in the 49 patients who underwent coronary angiography for different reasons at an average of  $41 \pm 17$  months after CABG were 98% for the LIMA-LAD anastomosis and 84% for the LIMA-diagonal anastomosis. Sequential anastomosis and individual anastomosis in patients undergoing CABG have been compared in many previous studies. A recent meta-analysis including nine cohorts, 7100 patients and 1440 grafts demonstrated that individual and sequential CABG were similar in terms of anastomosis patency and in-hospital mortality [25]. Additionally, in a study the mid- and long-term patency of sequential grafts appears to be better than single graft anastomosis (18). Given the lack of superiority of sequential anastomosis over individual anastomosis shown in meta-analysis, we consider that the favorable outcomes concerning postoperative stroke and hemodynamics observed in the present study are associated with the aortic no-touch technique and better preservation of myocardial perfusion achieved with off-pump CABG.

Neutrophils, and novel inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), the systemic inflammatory response index (SIRI – quotient of neutrophils and monocytes, divided by lymphocyte count) and systemic inflammatory index (SII – quotient of neutrophils and platelets divided by lymphocyte count) have documented value for predicting survival and mortality [26]. To rule out the risk of inflammatory activation that is secondary to cardiopulmonary bypass application, off-pump coronary artery bypass can be an alternative. When combined with

preoperative characteristics, these inflammatory indicators represent good prediction for long-term survival and mortality after off-pump coronary artery bypass surgery. In a recent study group comprising 538 patients who underwent off-pump coronary artery bypass surgery with a mean follow-up of  $4.7 \pm 1.7$  years, Urbanowicz *et al.* reported that multivariable analysis identified levels of neutrophils above  $4.3 \times 10^9/l$  (hazard ratio 13.44, 95% confidence interval 1.05–3.68,  $p = 0.037$ ), values of SIRI above 5.4 (hazard ratio 0.29, 95% confidence interval 0.09–0.92,  $p = 0.036$ ) and values of NLR above 3.5 (hazard ratio 2.21, 95% confidence interval 1.48–3.32,  $p = 0.001$ ) as being significant predictors of long-term mortality [26]. The authors also reported that the multifactorial models revealed the possibility of strong prediction by combining preoperative factors (chronic obstructive pulmonary disease, stroke, peripheral artery disease and preoperative platelets to lymphocyte ratio) and postoperative neutrophil counts ( $p = 0.0136$ ) or NLR ( $p = 0.0136$ ) or SIRI ( $p = 0.0136$ ). The authors also reported that although it was not confirmed in multivariable analysis, an SII above 953 was significant for long-term mortality predictions in the univariate analysis. Although these inflammatory indicators were not used in our study, we think that these new inflammatory indicators should be used in studies to demonstrate the superiority of off-pump coronary artery bypass surgery.

In brief, the most devastating complication and the weakest point – *the reason for pushing patients toward PCI* – of the coronary surgery is stroke. The LIMA has the most satisfactory patency rates; so with sequential anastomosis we can use the LIMA for both the LAD and diagonal artery. We have to improve and advance the no-touch techniques to reduce the rate of stroke so off-pump surgery may be a good alternative.

We consider that we avoid “touching and manipulating the aorta” by carrying out off-pump surgery and sequential anastomosis technique; and besides, we have the chance and possibility of using the best arterial graft for both the LAD and diagonal artery. We believe that both the favorable and satisfactory patency rate of LIMA-LAD anastomosis and the reduced rate of stroke – *the most devastating complication and the reason for pushing patients toward PCI* – are important for this technique.

There are some limitations to be mentioned regarding our study. The retrospective design of the present study does not allow us to present data concerning the mid- or long-term results of the off-pump CABG procedure with the aortic no-touch technique. Lack of a control group consisting of patients undergoing conventional CABG is another drawback of our study. Finally, the patency of the LAD artery or diagonal artery anastomoses was evaluated only in a small group of the study population. These results therefore need to be interpreted with caution.

## Conclusions

Off-pump CABG with sequential LIMA-diagonal artery-LAD anastomosis is associated with favorable postopera-

tive outcomes including reduced postoperative stroke, renal dysfunction, IABP, and inotropic agent requirement. Preoperative LVEF and presence of recent myocardial infarction are related to the postoperative need for IABP insertion and inotropic agent requirement and also the prevalence of acute renal failure. Our findings demonstrate that off-pump CABG in combination with the aortic no-touch technique provides excellent postoperative outcomes.

## Disclosure

The authors report no conflict of interest.

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